	Diethylene triamine penta(methylene phosphonic acid), 2Na Salt	ICCA	04/1	SIAM-18	-
	Diethylene triamine penta(methylene phosphonic acid), Na Salt	ICCA	04/1	SIAM-18	-
	Diethylene triamine penta(methylene phosphonic acid), 4Na Salt	ICCA	04/1	SIAM-18	-
	Diethylene triamine penta(methylene phosphonic acid), 3Na Salt	ICCA	04/1	SIAM-18	-
	Diethylene triamine penta(methylene phosphonic acid), 8Na Salt	ICCA	04/1	SIAM-18	-

- UNITED STATES

CAS_NO Category	SYNONYM	Additional Sponsor	Selection (year/month)	SIAM	Expected date for receipt of docs. (as of former info.)*
67561	Methanol	ICCA	02/8	SIAM-19	
78842	iso-Butanal		90/4	SIAM-5	November 2004
78922	sec-Butyl alcohol	ICCA	00/11	SIAM-14	June 2005
78933	Methyl ethyl ketone		91/9	SIAM-6	February 2005
96184	1,2,3-Trichloropropane	ICCA	00/11	SIAM-18	-
96297	2-Butanone oxime	JP, ICCA	97/4	SIAM-17	August 2005
96333	Methyl acrylate	ICCA	00/9	SIAM-16	July 2005
106310	Butyric anhydride	ICCA	00/11	SIAM-16	August 2005
106638	Acrylic acid, iso-butyl ester	ICCA	00/9	SIAM-15	July 2005
107926	Butyric acid	ICCA	00/11	SIAM-16	August 2005
108101	M.I.B.K		91/9	SIAM-5	December 2004
109999	Tetrahydrofuran		95/8	SIAM-10	March 2005
110190	Isobutyl acetate	ICCA	00/11	SIAM-17	September 2005
116154	1-Propene, hexafluoro	IT	90/4, 91/12	SIAM-8+10	April 2005
123386	Propanal		90/4	SIAM-1+3 (+4)	March 2005
123728	n-Butanal Butyraldehyde		91/12	SIAM-5	February 2005
123864	Butyl acetate	ICCA	95/8	SIAM-13	May 2005
140885	Ethyl acrylate	ICCA	00/9	SIAM-18	-
141786	Ethyl acetate	ICCA	95/8	SIAM-14	June 2005
141797	3-Penten-2-one, 4-methyl- Mesityl oxide		91/12	SIAM-6	February 2005
149575	Hexanoic acid, 2-ethyl-	SE	91/9	SIAM-9	May 2005
6422862	Terephthalic acid, bis(2-ethylhexyl) ester	ICCA	03/1	SIAM-17	October 2005
Category	Isobutyl acid	ICCA	00/11	SIAM-17	October 2005

Isobutyric Acid/Anhydride	Isobutyric anhydride	ICCA	00/11	SIAM-17	October 2005
Category Xylenes	o-Xylene	HU, ICCA	03/1	SIAM-16	September 2005
	p-Xylene	HU, ICCA	03/1		
	m-xylene	HU, ICCA	03/1		
	Xylene(s)	HU, ICCA	99/6		
Category Maleic Anhydride and Acid	Maleic anhydride	ICCA	00/9	SIAM-18	-
	Maleic acid	ICCA	04/1	SIAM-18	-
Category Propylene glycol phenyl ethers	2-Propanol, 1-phenoxy-	ICCA	00/9	SIAM-18	-
	Propylene glycol phenyl ether (beta isomer - primary alcohol)	ICCA	04/1	SIAM-18	-
	Propylene glycol phenyl ether (mixed isomer product)	ICCA	04/2	SIAM-18	-
Category Short Chain Alkyl Methacrylates Esters	Methacrylic acid, ethyl ester	JP,ICCA	00/9	SIAM-18	-
	iso-Butyl methacrylate	JP,ICCA	00/9	SIAM-18	-
	Butyl methacrylate	JP,ICCA	97/4	SIAM-18	-
	2-Ethylhexyl methacrylate	JP,ICCA	97/4	SIAM-18	-
Category Monoethylene	2-Butoxyethanol	ICCA	04/7	SIAM-19	-
	2-Butoxyethyl acetate	ICCA	00/9	SIAM-19	-
	Ethanol, 2-(hexyloxy)-	ICCA	00/9	SIAM-19	-
	Ethanol, 2-propoxy-	ICCA	97/4	SIAM-19	-
Category Higher olefins	1-Octadecene	ICCA	00/11	SIAM-19	-
	1-Hexadecene	ICCA	00/11	SIAM-19	-
	Hexene	ICCA	00/11	SIAM-19	-
	Decene	ICCA	04/7	SIAM-19	-
	Heptene	ICCA	00/11	SIAM-19	-
	Octene	ICCA	00/11	SIAM-19	-
	Dodecene	ICCA	00/11	SIAM-19	-
	Nonene	ICCA	00/11	SIAM-19	-
	Alkenes, C10-13	ICCA	04/7	SIAM-19	-

* Actual dates for each chemical or category may differ; however, the U.S. will aim to complete two per month.

Alpha-Olefins	1120361	1-Tetradecene	This profile includes an evaluation of SIDS-level testing data, using a category approach, with five individual monoolefins (1-hexene, 1-octene, 1-decene, 1-dodecene, and 1-tetradecene). For the purposes of the OECD SIDS Programme, the category was defined as olefins bearing a single medium-length (C6 – C14), even-numbered, unbranched aliphatic chain with no other functional groups. A category analysis was done for all the SIDS endpoints by examining available data to determine whether the proposed test plan – to treat the five chemicals as a category – was satisfactory. Results indicate that they were and so no further SIDS-level testing is necessary. The data indicate an increasing or decreasing trend or pattern from the shortest category member (C6) to the longest category member (C14) for various physicochemical properties and ecotoxicity (using a mixture of experimental data and estimation techniques), whereas there appears to be no difference across category members for biodegradation and health endpoints. Melting point, vapor pressure, and water solubility decrease with increasing chain length while boiling point and octanol:water partition coeff Given the fact that not all category members were tested for each *SIDS endpoint, this analysis shows that where test data exist for more th*
	872059	1-Decene	
	112414	1-Dodecene	
	592416	1-Hexene	
	111660	1-Octene	
Amorphous silica silicates	112926008	Silica gel, crystal-free	The similarity in the chemical structure, composition, production and processing as well as the similarity in physico-chemical properties and the available toxicological and health data, strongly suggest that the impact on the living organism and environment should not differ *considerably between the category members: synthetic amorphous silica (SAS)* [CAS No 7631-86-9] and synthetic amorphous silicates, Na-Al silicates (NAS) [CAS No 1344-00-9] and Ca silicates (CS) [CAS No 1344-95-2]. They all form fine powders of amorphous particles between 1 and 350 µm with high surface areas.
	1344009	Silicic acid, aluminium sodium salt	
	112945525	synthetic amorphous silica	
	1344952	Silicic acid, calcium salt	
	7631869	Silicon dioxide	
Benzene, C10-C16 Alkyl derivates (LAB)	129813598	Benzene, mono C12-14 alkyl derivs.	The information of this category rational is not recorded because of old evaluation
	6742547	Benzene, undecyl-	
	68442693	Benzene, mono C10-14 alkyl derivs.	
	123013	*Dodecylbenzene*	
	129813587	Benzene, mono C10-13 alkyl derivs.	
	68648873	Benzene, C10-C16 alkyl derivs	
	129813601	Benzene, mono C14-16 alkyl derivs.	
Benzoates	532321	Sodium benzoate	The benzyl alcohol, benzoic acid and its sodium and potassium salt can be considered as a single category regarding human health, as they are all rapidly metabolised and excreted via a common pathway within 24hrs. Systemic toxic effects of similar nature (e.g. liver kidney) were observed. However with the benzoic acid and its salts at higher doses than the benzyl alcohol. *For environmental effects* the category is less clear, however all are readily biodegradable, non-bioaccumulative and acute toxicity values are similar. For human health all exposure routes are possible, despite benzoic acid and its salts are solids and benzyl alcohol is a liquid. For workers it will *mainly be by inhalation and by skin, whereas for consumers it will mainly be oral and dermal.*
	582252	Potassium benzoate	
	100516	Benzylalcohol	
	65850	Benzoic acid	
Butanedioic acid	150903	Butanedioic acid, disodium salt	Analogue Rationale Disodium succinate is stable as a hexahydrate and has been produced as disodium succinate hexahydrate (CAS No.: 6106-21-4) in Japan. Many toxicity studies were conducted using disodium succinate hexahydrate as the test substance, because there should be no difference between disodium suucinate and disodium succinate hexahydrate in terms of environmental behavior, aquatic toxicity, and mammalian toxicity.
Butenes	115117	Iso-Butylene 2-Methylpropene	The Butenes Category includes six CAS numbers that are similar from a process and toxicology perspective. Each substance within this category is a C4 olefin or contains a mixture of selected C4 olefins that are produced from a reaction and/or separation activity in an *olefins chemical plant. Four CAS numbers describe different C4 isomers,* each is a hydrocarbon with the same chemical formula and one double bond between two carbon atoms. Two CAS numbers describe mixtures of C4 olefins that contain either two or all four different isomers. The six substances share relatively similar physico-chemical properties, which suggests that their environmental fate will be similar. The chemicals are expected to have similar kinetic properties because of similar physical-chemical properties. No specific target organ was identified and no or minimal changes in body weight were found at the highest dose only for all the butenes. Therefore the butenes can be treated as a category.
	590181	2-Butene, (2Z)-	
	624646	2-Butene, (2E)-	
	25167673	Butene	
	106989	1-Butene	
	107017	2-Butene	
Butyl Series Metabolic Category	107926	Butyric acid	The n-Butyric Acid/n-Butyric Anhydride Category consists of two sponsored chemicals: n-butyric acid (CAS No. 107-92-6), and n-butyric anhydride (CAS No. 106-31-0.) The category members are closely related since the anhydride rapidly hydrolyzes in the presence of water to form the acid. *Since testing of the anhydride is in reality testing of the acid form, these materials share toxicity characteristics* and form the basis of the category. As a result, the metabolic series approach can be used to address the non-acute health endpoints. *In addition, increased blood levels of n-butyric acid have been demonstrated following administration of the metabolic precursors of* butyric acid (n-butyl acetate and n-butanol.) Since the increased blood levels of n-butyric acid following n-butyl acetate and n-butanol have been demonstrated experimentally, hazard identification studies using either n-butyl acetate or n-butanol exposures have been used to identify the hazards associated with systemic exposure to n-butyric acid. Therefore, data from n-butyl acetate (CAS No. 123-86-4) and/or n-butanol (71-36-3) are used as analogs to either address or supplement the respective systemic toxicity endpoints for n-butyric Based on hydrolysis data, the acute aquatic toxicity endpoints of both n-butyric acid and n-butyric anhydride have been addressed using d
	106310	Butyric anhydride	
Cadmium (oxide)	1306190	Cadmium oxide	The main reason for treating Cadmium (i.e. cadmium metal) and Cadmium oxide together stems from consideration of similar physico-chemical properties, in particular their relatively low solubility in water and from consideration of the conditions of exposure. Indeed, in occupational settings, workers are mainly exposed to cadmium oxide fumes and dust, produced when the metal is heated. The general population is exposed mainly by the oral route via food or water to cadmium (not necessarily CdO/Cd metal). However, both compounds release the biologically active form, i.e. ionic Cd2+ in the environment and biological tissues and so the effects can generally be treated together. The objective of the study was not to be complete in reviewing the data on cadmium compounds but rather to focus on critical studies and endpoints. Reviews have been used in retrieving critical studies.
	7440439	Cadmium	
Chromates	7789095	Ammonium dichromate	These five chromium (VI) substances have been assessed as a group, since after release to the environment the chromium species produced are the same from each substance, and so the fate and effects in the environment can be considered together. Similarly for *human health, the species produced will behave similarly in biological tissues and so the effects can be treated as a group.* (There is also an additional concern about the acidity of solutions of chromium trioxide.)
	10588019	Sodium dichromate	
	7775113	Sodium chromate	
	7778509	Potassium dichromate	
	1333820	Chromium trioxide	
C.I. Fluorescent Brightener 28/113	70942017	Potassium sodium 4,4'-bis[6-anilino-4-[bis(2-hydroxyethyl)amino]-1,3,5-triazin-2-yl] amino]stilbene-2,2'-*disulphonate (C.I.* Fluorescent Brightener 28/113)	C.I. Fluorescent Brightener 28/113 is a technical product which is manufactured as the potassium/sodium salt (CAS No. 70942-01-7), dipotassium salt (CAS No 71230-67-6), disodium salt (CAS No. 4193-55-9), and free acid (CAS No. 4404-43-7). All these types of C.I. *Fluorescent Brightener 28/113 are based on the identical organic disulfonates which determines the ecological and the toxicological* properties. Additionally there are a number of very similar fluorescent whitening agents with only minor differences of the structure and very similar physical and chemical properties. Data from these substances have been used to bridge possible data gaps in the section "*Human health*": (C.I. Fluorescent Brighteners 24, 220, 225, and the Fluorescent Brightener 4,4'-bis[4-anilino -6-[(2-hydroxyethyl)methyl-amino]-s-triazin-2-yl)amino]2,2'-stilbenedisulphonate = CAS No. 12224-02-1, 16470-24-9, 24019-80-5, and 13863-31-5, respectively).
	71230676	Dipotassium salt 4,4'-bis[6-anilino-4-[bis(2-hydroxyethyl)amino]-1,3,5-triazin-2-yl] amino]stilbene-2,2'-disulphonate	

Diginent Sh/113	4193559	Disodium salt 4,4'-bis[6-anilino-4-[bis(2-hydroxyethyl)amino]-1,3,5-triazin-2-yl] amino]stilbene-2,2'-disulphonate	
	4404437	Benzenesulfonic acid, 2,2'-(1,2-ethenediyl)bis[5-[[4-[bis(2-hydroxyethyl)amino]-6-(phenylamino)-1,3,5-triazin-2-yl]amino]-	
Diarylide Yellow pigments	5102830	Pigment yellow 13	The Diarylide Yellow Pigments category includes molecules with similar chemical structure; all contain the chloro-substituted biphenyl moiety, azo-moieties, keto groups and a substituted or non-substituted phenyl ring at both ends of the molecule, which is connected to the central part of the molecule via an amide bond. The only difference is in the substitution of the outer aniline rings, e.g. methyl, chloro and methoxy. They are expected to display essentially the same trend in environmental, ecotoxicological and toxicological behaviour based on the available data.
	6358856	Pigment yellow 12	
	5567157	Pigment yellow 83	
Diethylene glycol ethers	112152	2-(2-Ethoxyethoxy)ethyl acetate	The category includes five diethylene glycol ethers or acetates (DGEE, DGEEA, DGPE, DGBEA and DGHE). The members of this category all have similar molecular structures, functionality and metabolic pathways and demonstrate similar physicochemical and environmental fate properties and mammalian toxicity. However, for aquatic toxicity, diethylene glycol ethers (DGEE, DGPE and DGHE) and diethylene glycol ether acetates (DGEEA and DGBEA) are considered separately because diethylene glycol ether acetates do not hydrolyze readily in water at environmental conditions. Three additional structural analogs are included to support this category. Each of them has previously been endorsed at a SIAM. The chemicals are: diethylene glycol butyl ether (DGBE, CAS No. 112-34-5; SIAM4), ethylene glycol hexyl ether (EGHE, CAS No. 112-25-4; SIAM19), and ethylene glycol butyl ether acetate (EGBEA, CAS No. 112-07-2; SIAM19). EGHE and EGBEA are members from the monoethelyene glycol ethers category. DGBE is included to fill data gaps for mammalian and aquatic toxicity and provide supplemental data for the other category members. The molecular weight of DGBE is in between DGPE and DGHE, and DGBEA is rapidly hydrolyzed to
	112594	Ethanol, 2-[2-(hexyloxy)ethoxy]-	
	111900	Ethanol, 2-(2-ethoxyethoxy)-	
	6881943	Ethanol, 2-(2-propoxyethoxy)-	
	124174	Ethanol, 2-(2-butoxyethoxy)-, acetate	
Ethylene glycols	107211	Ethylene glycol	Category members are represented by the generic molecular structure, HO(CH2 CH2 O) n H, where n = 1-5. All category members therefore possess two terminal hydroxy groups and the members differ from each other only in the number of oxyethylene units. Because of this it is appropriate to classify EG and the higher glycols (up to and including n=5) as a single group. At n = 6-8, absorption from ingestion decreases and certain physicochemical attributes change significantly. Adequate studies are available for most of the required SIDS endpoints for the category members. A category approach is used where experimental data are not available. Category members ethylene glycol and the higher glycols (di-, tri-, tetra-, and penta-) are closely related in structure and have physicochemical properties which differ in a regular and expected way as a result of increasing molecular weight and consistent functionality of a relatively less stable hydroxy moiety on each end of the molecule. Thus, the hazard profile and dose response are also expected to change consistently, with decreasing potential for adverse effect with increasing molecular weight. Available data and quantite Available data and modeling confirm that as the molecular weight increases, the potential for systemic, reproductive, and developmental to
	111466	Diethylene glycol (DEG)	
	112276	Triethylene glycol	
	112607	Tetraethylene glycol	
	4792158	Pentaethylene glycol	
Gluconates	526954	D-Gluconic acid	Gluconate derivatives are presented as a category. Gluconic acid and its mineral salts freely dissociate to the gluconate anion and the respective cations. Glucono-delta-lactone (GDL), the 1,5-inner ester of gluconic acid, is formed from the free acid by the removal of water. On the basis of these spontaneous chemical rearrangements, glucono-delta-lactone, gluconic acid and its sodium, calcium and potassium salts can be considered as a category, with all members sharing the same representative moiety, the gluconate anion. Manufacturing and uses of the category members are also interlinked. The data summarized in this report are focused on the environmental and health effects from the gluconate anion and read-across to the lactone but do not deal with specific effects of the cations. Thus toxicological effects related to the cationic components are not part of the present report.
	299274	Potassium gluconate	
	18016245	Calcium gluconate	
	90802	D-Glucono-1,5-lactone	
	299285	Calcium gluconate	
	527071	Gluconic acid, monosodium salt	
High Boiling EGE's	1559348	3,6,9,12-tetraoxahexadecan-1-ol	The category contains three structurally related, high boiling glycol ethers: • Triethylene glycol butyl ether (TGBE; CAS No. 143-22-6); • Tetraethylene glycol methyl ether (TetraME; CAS No. 23783-42-8); and • Tetraethylene glycol butyl ether (TetraBE; CAS No. 1559-34-8). TGBE is available as a relatively pure product, with a purity of >85 percent. TetraME and TetraBE are not commercially available as pure compounds, but as components of mixtures that contain glycol ethers of various chain lengths. Data for these glycol ethers are supplemented with data from compounds that are closely related to the category members in molecular structure, and physicochemical properties, and toxicity. These compounds are: • Triethylene glycol methyl ether (TGME; CAS No. 112-35-6); • Triethylene glycol ethyl ether (TGEE; CAS No. 112-50-5); • Polyethylene glycol methyl ether (MPEG350; CAS No. 9004-74-4); • Polyethylene glycol butyl ether (CAS No. 9004-77-7); and • Brake Fluid DOT 4. TGME and TGEE were both reviewed at SIAM 4. Polyethylene glycol monobutyl ether (CAS No. 9004-77-7) is used only for the melting point. (Details of the composition of category members and analogs are provided in Section 1 and Appendix I of the SIAR.)
	143226	Triethyleneglycol, monobutylether	
	23783428	2,5,8,11-Tetraoxatridecan-13-ol	
High Molecular Weight Phthalate Esters	53306540	1,2-benzenedicarboxylic acid, di-2-propylheptyl ester	The High Molecular Weight Phthalate Ester (HMWPE) Category consists of esters with an alkyl carbon backbone with 7 carbon (C) atoms or greater. The category is formed on the principle that substances of similar structure have similar environmental and toxicological properties. Data are available on substances that meet the category definition and which are, or are not members of the category, to demonstrate that the members of this category have similar biological activities and that, when used, read-across is an appropriate approach to characterize endpoints for select members of this category. The HMWPE Category contains chemically similar substances, 1,2-benzenedicarboxylic acid reacted with branched and/or linear alkyl alcohols, which are referred to as the alkyl chains in the phthalate ester molecule. A phthalate ester (PE) molecule is produced by esterifying one molecule of benzenedicarboxylic acid (phthalic anhydride) with two alcohol molecules. The seven members of this category contain linear and/or branched diheptyl, dioctyl, dinonyl, didecyl, diundecyl, didodecyl, and/or ditridecyl PEs. The branched alkyl chains are composed of varying mixed isomers. The length of the alkyl chains varies by substance, but the total carbon number of the long Due to similar chemical structure, category members are generally similar with respect to select physico-chemical properties or display an For PEs, the critical toxicological effects are development and reproduction. These aspects are very structure dependent, and are associat As mentioned, DINP and DIDP, meet the category definition in that their backbone lengths are predominantly C7 or above, and produce litt To correctly characterize selected endpoints for PEs, read-across techniques can be applied. Read-across is typically performed using me Two general rules for read-across as they apply to PEs include: • Chemical relatedness - the substance without data as well as the substance(s) with data are similar such that their physicochemical, biolo • Structural similarity - the substance without data possesses small incremental structural differences from the reference substance(s) or th For PEs in general, read-across can be applied across increasing/decreasing carbon (C) numbers in the alkyl side-chains. For example, de
	3648202	Di-undecyl phthalate	
	68515413	Phthalic acid, di-C7-9-branched & linear esters	
	85507795	Diundecyl phthalate, branched and linear esters	
	68515479	Phthalic acid, di-C11-14-branched alkyl esters C13 rich	

	119062	Ditridecyl phthalate	• Di-phC10 PE (CAS No 53306-54-0) • Di-C7-9 PE (CAS No 68515-41-3) • Di-C11 PE (CAS No 3648-20-2 or 85507-79-5) • Di-C9-11 PE (CAS No 68515-43-5) • Di-C13 PE (CAS No 68515-47-9 or 119-06-2)
	68515435	Phthalic acid, di-C9-11-branched & linear alkyl esters	
Higher olefins	25264931	Hexene	This profile includes an evaluation of SIDS-level testing data, using a category approach, with six individual internal olefins (C6 – C10 and C12), a C10 – 13 internal olefins blend and two linear alpha olefins (1-hexadecene and 1-octadecene), all of which are mono-olefins. The internal olefins are predominantly linear, but may contain small amounts of branched materials. For the purposes of the OECD HPV *Chemicals Programme*, the category was defined as "Higher Olefins." The category designation was based on the belief that internalizing the location of the carbon-carbon double bond, increasing the length of the carbon chain, and/or changing the carbon skeleton's structure *from linear to branched does not change the toxicity profile*, or changes the profile in a consistent pattern from lower to higher carbon numbers. While the category is actually defined as C6 – C18 mono-olefins (sponsored chemicals), we included surrogate data from a *mixed stream containing C20-C24 linear and branched internal* olefins. While we realize that sufficient data exist to support the category without the data on the C20-C24, we believe these data provide additional support and strengthen the hypothesis that changing carbon nu
	25339564	Heptene	
	25377837	Octene	
	629732	1-Hexadecene	
	25339531	*Decene*	
	85535871	Alkenes, C10-13	
	25378227	Dodecene	
	27215958	Nonene	
	112889	1-Octadecene	
Hydrotope Surfactants	32073226	Benzene, (1-*methylethyl*)-, monosulfo deriv., *sodium salt*	Hydrotropes are supported as a category because of the close consistency of the compounds, their commercial uses, fate, and health *and environmental effects*. The hydrotropes are used as coupling agents to solubilize the water insoluble and often incompatible functional ingredients of household and institutional cleaning products and personal care products. These hydrotropes are not *surfactants but are used to solubilize complex formulas* in water. They function to stabilize solutions, modify viscosity and cloud-point, limit low temperature phase separation and reduce foam formation. Manufactured products are used as aqueous solutions (30-60% *active substance) or as granular* solids containing 90-95% active substance. *The hydrotropes category may be initially considered* as three sub-groups: the methyl, dimethyl and methylethyl benzene sulfonates, (or the toluene, xylene and cumene sulfonates). Although the counter ion will also determine the physical and chemical behavior of the *compounds, the chemical reactivity and classification for* this purpose is not expected to be effected by the difference in counter ion (i.e., Na+, NH4+, Ca++, or K+). Note that two of the compounds (xylene and cumene sulfonic acid, sodium salts) have more than one CAS num In general, the presence of one or two methyl groups or a methylethyl group on the benzene ring is not expected to have a significant influe It was therefore concluded that the three sub-groups are expected to be generally comparable and predictable in their chemical behavior (
	37475880	Benzenesulfonic acid, (1-methylethyl)-, ammonium salt	
	28348530	Sodium cumenesulfonate	
	12068030	Benzenesulfonic acid, methyl-, sodium salt	
	1300727	Benzenesulfonic acid, *dimethyl-, sodium salt*	
Isobutyric Acid/Anhydride	79312	Isobutyl acid	The category members isobutyric acid (CAS No. 79-31-2), and isobutyric anhydride (CAS No. 97-72-3) *are closely related since the* anhydride rapidly hydrolyzes in the presence of water to form the acid. Since testing of the anhydride is in reality testing of the acid form, these materials share toxicity characteristics and form the basis of the category. As a result, the *metabolic series approach can be used* to address the non-acute health endpoints. Increased blood levels of isobutyric acid have been demonstrated following administration of isobutanol, a metabolic precursor of isobutyric acid. Hazard identification studies using isobutanol exposures have been used to *identify the hazards associated with* systemic exposure to isobutyric acid. Therefore, isobutanol (78-83-1) is used as an analog to either address or supplement the respective systemic toxicity endpoints for isobutyric acid.
	97723	Isobutyric anhydride	Based on hydrolysis data, the acute aquatic toxicity endpoints of both isobutyric acid and isobutyric anhydride *have been addressed* using data from structural analogs, alleviating the need for additional testing on isobutyric acid. As a result, available data from propionic a
Linear Alkylbenzene Sulfonates	90194459	Benzenesulfonic acid, mono-C10-13-alkyl derivs., sodium salts	The LAS molecule contains an aromatic ring sulfonated at the para position and attached to a linear alkyl chain at any position except the terminal carbons. The alkyl carbon chain typically has 10 to 14 carbon atoms and the linearity of the alkyl chains ranges from 87 to 98%. While commercial LAS consists of more than 20 individual components, the ratio of the various homologs and isomers, representing different alkyl chain lengths and aromatic ring positions along the linear alkyl chain, is relatively constant in currently produced products, with the weighted average carbon number of the alkyl chain based on production volume per region between 11.7-11.8. LAS are supported as a category because of the close consistency of the mixtures, their commercial uses, fate, and health and environmental effects. LAS is the primary cleaning agent used in many laundry detergents and cleaners at concentrations up to 25 percent in consumer products, and up to 30 percent in commercial products, with the exception of one reported product at 45% percent in concentrated solid form that is mechanically dispensed into diluted solution for dishwashing.
	68081812	Benzenesulfonic acid, *mono-C10-16-alkyl*	
	1322981	Benzenesulfonic acid, decyl-, Na salt	
	127184525	4-C10-13-sec Alkyl deriv benzene sulfonic acid, sodium salt	
	68411303	Benzenesulfonic acid, C10-13-alkyl derivs.	
	27636755	Benzenesulfonic acid, undecyl-, Na salt	
	26248248	Benzenesulfonic acid, tridecyl-, Na salt	
	25155300	Benzenesulfonic acid, *dodecyl-, Na salt*	
	69669449	C10-14 Alkyl deriv benzene sulfonic acid, sodium salt	
	85117506	Benzenesulfonic acid, mono-C10-14-alkyl	
m,p-Cresols	106445	Phenol, 4-methyl-	m-Cresol, p-cresol and mixtures of both isomers can be considered as a single category *because of their similarity in physico-chemical* properties, distribution between environmental compartments, degradation, ecotoxicity, and toxicology.
	15831104	m-, p-Cresol	
	108394	1,3-Cresol	
Maleic Anhydride and Acid	110167	Maleic acid	*Maleic anhydride is readily hydrolyzed to maleic acid under aqueous conditions.* As a result, these two chemicals are presented because of the conditions used to test their toxicity. The only difference may be due to the potential for maleic anhydride to form haptens by *acylating with amino acids, resulting in an immunological response* (dermal and respiratory sensitization).
	108316	Maleic anhydride	
Malonates	108598	Dimethyl malonate	The production and use pattern of Diethylmalonate (DEM) and Dimethylmalonate (DMM) are comparable. The two chemicals have very similar physico-chemical properties and both esters are hydrolyzed via a two step reaction to malonic acid and the corresponding alcohol, methanol or ethanol. It is likely that unspecific esterases in the body catalyze the hydrolysis. The alcohols and malonic acid are physiological substances that are metabolized via physiological pathways. Ethanol (CAS No. 64-17-5) and methanol (CAS No. 67-56-1) were assessed at SIAM 19. For ethanol it was concluded that the chemical is currently of low priority for further work, because the hazardous properties of ethanol are manifest only at doses associated with consumption of alcoholic beverages. As it is impossible to reach these exposure levels as a consequence of the manufacture and use of malonates, it can be expected that malonic acid will be the metabolite that determines the toxicity of DEM. For methanol, SIAM 19 decided that this chemical is a candidate for further work. Methanol exhibits potential hazardous properties for human health (neurological effects, CNS depression, ocular effects, reproductive and
	105533	Diethyl malonate	
Menthols (with non-HPVCs: 89781, 2216515 & 15356602)	89781	D/L-Menthol	The menthols category is comprised of the isomers L-menthol, D-menthol, the racemate and menthol (unspecified isomers). The menthols can be considered as a category because of their similarity in physico-chemical, toxicological, ecotoxicological and environmental fate properties.
	15356602	(+)-Menthol	
	2216515	L-Menthol	
	1490046	DL-menthol	
Methylenediphenyl diisocyanates	26447405	Benzene, 1,1'-methylenebis(isocyanato-	The predominant commercial product covered by the term MDI is the liquid reaction mixture produced from methylene di-aniline. It comprises 4,4'-MDI and its oligomers with small amounts of the other monomers 2,4-MDI and 2,2'-MDI. It is commonly termed 'polymeric MDI' also called 'generic', 'crude' or 'non-isomer specific' MDI. A relatively small proportion is converted to monomeric MDI (essentially 4,4'-MDI) by purification. The data-set on this 'generic MDI' covers also the testing results on the other MDI analogues. The category approach is considered justified since the substances have closely related composition i.e. excess of monomeric MDI as well as comparable –NCO content that are considered as the primary determinants of (eco)toxicity.
	9016879	*(polymeric)* M.D.I.	
	5873541	2,4'-M.D.I.	
	101688	4,4'-M.D.I.	

	2536052	2,2'-M.D.I.	
Monoethylene glycol ethers	111762	2-Butoxyethanol	The four substances of this category all have similar molecular structures, functionality and metabolic pathways. The category members demonstrate similar physicochemical properties and mammalian toxicity. EGBE is included in the category only to fill data gaps for mammalian toxicity. A separate dossier on EGBE is not included as this chemical's data set was previously agreed to at SIAM 6. The reader should refer to the existing SIDS dossier for additional information on EGBE. The acetylated glycol ether, EGBEA, although rapidly metabolized in vivo to its corresponding glycol ether, is not expected to hydrolyze rapidly to EGBE in the aqueous environment. Therefore, EGBEA aquatic toxicity data are not extrapolated to the other category members.
	2807309	Ethanol, 2-propoxy-	
	112072	2-Butoxyethyl acetate	
	112254	Ethanol, 2-(hexyloxy)-	
Persulfates	7775271	Disodium peroxydisulfate	The persulfates category includes molecules with similar chemical structure and similar physical-chemical properties. The inorganic substances differ only by the cationic portion of the salt, which is not expected to influence the hazardous properties of the molecule. The anionic part is identical and, therefore, the three salts are expected to display the same environmental, ecotoxicological and toxicological behaviour based on the available data.
	7727211	Dipotassium peroxodisulphate	
	7727540	Diammonium peroxydisulfate	
Phosphonic acids - Group 1	94021235	Amino tris(methylenephosphonic acid), 4Na Salt	This category covers a phosphonic acid and various sodium salts of that acid. The different salts are prepared by neutralising the acid to a specific pH. Data are available for the acid and some salts. The substances are commercially available as aqueous solutions only and in an environmental context the speciation will be the same. In the present context the effect of the counter-ion (sodium) will not be significant. The properties of the members of the category are consistent across all end points. The category is expressed as Phosphonic Acid Compounds Group 1 because two other groups have been identified, with close structural analogy to the present one. Group 2 is 1-Hydroxy-1,1-ethane-diphosphonic acid (CAS 2809-21-4) and its sodium and potassium salts; Group 3 is Diethylene triamine penta(methylene phosphonic acid) (CAS 15827-60-8) and its sodium salts.
	7611509	Amino tris(methylenephosphonic acid), 3Na Salt	
	20592852	Phosphonic acid, [nitrilotris(methylene)]tris-, sodium salt	
	0	Amino tris(methylenephosphonic acid), Na Salt	
	2235430	Phosphonic acid, [nitrilotris(methylene)]tris-, pentasodium salt	
	15505052	Amino tris(methylenephosphonic acid), 6Na Salt	
	4105015	Amino tris(methylenephosphonic acid), 2Na Salt	
	6419198	Tris(phosphonomethyl)amine	
Phosphonic acids - Group 2	17721721	1-Hydroxy-1,1-ethane-diphosphonic acid, K Salt	This category covers a phosphonic acid and sodium salts of that acid. The different salts are prepared by neutralising the acid to a specific pH. Data are available for the acid and some salts. The substances are commercially available as aqueous solutions only and in an environmental context the speciation will be the same. In the present context the effect of the counter-ion (sodium/potassium) will not be significant. The properties of the members of the category are consistent across all end points. The category is expressed as Phosphonic Acid Compounds Group 2 because two other groups have been identified, with close structural analogy to the present one. Group 1 is Amino tris(methylenephosphonic acid) (6419-19-8) and its sodium salts; Group 3 is Diethylene triamine penta(methylene phosphonic acid) (CAS 15827-60-8) and its sodium salts.
	60376081	1-Hydroxy-1,1-ethane-diphosphonic acid, 3K Salt	
	7414837	Disodium dihydrogen (1-hydroxyethylidene)bisphosphonate	
	29329713	Phosphonic acid, (1-hydroxyethylidene)bis-, sodium salt	
	67953768	Phosphonic acid, (1-hydroxyethylidene)bis-, potassium salt	
	17721685	1-Hydroxy-1,1-ethane-diphosphonic acid, Na Salt	
	2666140	1-Hydroxy-1,1-ethane-diphosphonic acid, 3Na Salt	
	21089065	1-Hydroxy-1,1-ethane-diphosphonic acid, 2K Salt	
	14860538	1-Hydroxy-1,1-ethane-diphosphonic acid, 4K Salt	
	87977580	1-Hydroxy-1,1-ethane-diphosphonic acid, 5K Salt	
	2809214	Phosphonic acid, (1-hydroxyethylidene)bis-	
	13710399	1-Hydroxy-1,1-ethane-diphosphonic acid, 5Na Salt	
	3794830	1-Hydroxy-1,1-ethane-diphosphonic acid, 4Na Salt	
Phosphonic acids -	95183543	Diethylene triamine penta(methylene phosphonic acid), 8Na Salt	This category covers a phosphonic acid and sodium salts of that acid. The different salts are prepared by neutralising the acid to a specific pH. Data are available for the acid and some salts. The substances are commercially available as aqueous solutions only and in an environmental context the speciation will be the same. In the present context the effect of the counter-ion (sodium) will not be significant. The properties of the members of the category are consistent across all end points. The category is expressed as Phosphonic Acid Compounds Group 3 because two other groups have been identified, with close structural analogy to the present one. Group 1 is Amino tris(methylenephosphonic acid) (6419-19-8) and its sodium salts; Group 2 is 1-Hydroxy-1,1-ethane-diphosphonic acid (CAS 2809-21-4) and its sodium and potassium salts.
	93841748	Diethylene triamine penta(methylene phosphonic acid), 6Na Salt	
	93841760	Diethylene triamine penta(methylene phosphonic acid), 10Na Salt	
	61792094	Diethylene triamine penta(methylene phosphonic acid), 5Na Salt	
	15827608	Phosphonic acid, [[(phosphonomethyl)imino]bis[2,1-ethanediylnitrilobis(methylene)]]tetrakis-	
	94987776	Diethylene triamine penta(methylene phosphonic acid), 4Na Salt	

Phosphonic acids - Group 3	94987754	*Diethylene triamine* penta(methylene phosphonic acid), 2Na Salt	
	94987765	Diethylene triamine penta(methylene phosphonic acid), Na Salt	
	22042962	Phosphonic acid, [[(phosphonomethyl)imino]bis[2,1-ethanediylnitrilobis(methylene)]]tetrakis-, sodium salt	
	93841759	Diethylene triamine penta(methylene phosphonic acid), 9Na Salt	
	68155782	Diethylene triamine penta(methylene phosphonic acid), 7Na Salt	
	95015066	Diethylene triamine penta(methylene phosphonic acid), 3Na Salt	
Propylene Glycol Ethers	5131668	2-*Propanol, 1-butoxy-*	*The category contains four structurally related propylene glycol ethers:* Propylene Glycol n-Butyl Ether (PnB, 5131-66-8, major ("alpha") isomer, 29387-86-8 isomeric mixture) Dipropylene Glycol n-Butyl Ether (DPnB, 29911-28-2 major isomer or 35884-42-5 isomeric mixture)) Dipropylene Glycol Methyl Ether Acetate (DPMA, 88917-22-0 isomeric mixture) Tripropylene Glycol Methyl Ether (TPM, 20324-33-8 one of the isomers and 25498-49-1 isomeric mixture) The alpha (secondary alcohol) form is kinetically favored during synthesis. PnB is available as the isomeric mixture in which the alpha isomer is the predominant isomer (ca. 95%. DPnB, DPMA and TPM are commercially produced as mixtures of isomeric components in which the internal ether linkages may be adjacent to either primary or secondary carbon atoms. Thus, for DPMA and DPnB the commercially produced products may contain up to 4 such isomers. In the case of TPM, the commercially produced product may contain up to 8 such isomers. Data for these propylene glycol ethers are supplemented with data from three propylene glycol ethers that are closely related to the category members in molecular structure, physicochemical properties and toxicity and thus extend the category. These compounds are: *Propylene Glycol Methyl Ether (PM; CAS No. 107-98-2)* Propylene Glycol Methyl Ether Acetate (PMA; CAS No. 108-65-6) Dipropylene Glycol Methyl Ether (DPM; CAS No. 34590-94-8 isomeric mixture and 20324-32-7 major isomer) PM and PMA were reviewed at SIAM 11 and DPM was reviewed at SIAM 12. All were assigned as low priority for further work.
	20324338	2-Propanol, 1-[2-(2-methoxy-1-methylethoxy)-1-methylethoxy_-	
	25498491	2-(2-methoxymethylethoxy)methylethoxy propanol	
	29911282	1-(2-butoxy-1-methylethoxy)propan-2-ol	
	88917220	Propanol, (2-methoxymethylethoxy)-, acetate	
	29387868	1-Propanol, butoxy-	
Short Chain Alkyl Methacrylates Esters	97881	Butyl methacrylate	The short chain (C2-C8) unsaturated linear and branched alkyl methacylates included in this category show Structure Activity Relationship with respect to environmental toxicity, distribution and fate, and mammalian toxicity. These esters are rapidly metabolized to *methacrylic acid (CAS 79-41-4) and the structurally corresponding alcohol by non-specific carboxylesterases in several tissues.* Methyl methacrylate (MMA) (CAS 80-62-6), the C1 ester, is the largest volume methacrylate ester that has been studied extensively and reviewed in the OECD HPV Chemicals Programme. As such, MMA provides a robust reference chemical for this category.
	688846	2-Ethylhexyl methacrylate	
	97869	Iso-Butyl methacrylate	
	97632	Methacrylic acid, ethyl ester	
Soluble Silicates	10213793	Disodium silicate, pentahydrate	The soluble silicates are structurally very similar. Silicon-oxide tetrahedra as the basic structural units are linked with each other via Si-O-Si bonds resulting in an infinite three-dimensional network. The negative charge of unshared oxygen atoms is balanced by the presence of sodium or potassium cations which are randomly speced in the interstices. The extent to which balancing alkali ions are present in a given silicate is defined by the molar ratio SiO2/M2O (M = Na or K). The higher the molar ratio, the less sodium or potassium ions are present in the silica network and consequently the less alkaline the silicates are. Whereas the sodium and potassium salts have an amorphous three-dimensional structure, the disodium salts (= metasilicate) are crystalline with penta- and nonahydrate differing from the anhydrous form only by their water of crystallisation. Once in aqueous solution, all soluble silicates are subject to the same molecular speciation resulting in a mixture of monomeric tetrahedral ions, oligomeric linear or cyclic silicate ions and polysilicate ions. At environmental pH values the soluble silicates are present as poorly soluble amorphous *silica and monomeric silicic acid. The biological pro*
	6834920	Disodium metasilicate (Na2SiO3)	
	1312761	Potassium silicate	
	13517243	Silicic acid, disodium salt, nonahydrate	
	1344098	*Sodium silicate*	
Xylenes	95476	o-Xylene	Ortho- meta- and para-xylene are chemical isomers, with the only difference being the position of the methyl group on the benzene ring. Mixed xylene is a mixture of the three isomers and in addition, typically contains 15-20% ethylbenzene. The xylene isomers have similar physicochemical properties with the exception perhaps of the higher melting point of p-xylene. In addition, the toxicity of the three individual isomers and mixed xylene is qualitatively similar.
	106423	p-Xylene	
	108383	m-xylene	
	1330207	Xylene(s)	
Zinc metal amd salts	91051013	Fatty acids, C16-18, zinc salts	The Zincs Category includes six CAS numbers that are similar from a hazard point of view. It is assumed that all zincs either dissociate or form the zinc cation that is responsible for the hazardous effects. In the environment the zinc cation is formed via several speciation or transformation reactions, while furthermore it is assumed that, where appropriate, the counter ion does not significantly attribute to the major effects seen. In the human health assessment of the hazards it is assumed that for systemic toxicity the hazardous properties can be attributed again to the zinc cation and the counter ion be ignored.
	7646857	Zinc chloride	
	1314132	Zinc oxide	
	557051	Stearic acid, zinc salt	
	7779900	Zinc orthophosphate Zn3(PO4)2	
	7733020	Zinc sulfate	
	7440666	Zinc	

Annex 5: The list of case studies

[Annex 5-1]　OECD 事例調査

[Annex 5-2]　米国事例調査　(新規化学物質)

[Annex 5-3]　欧州　(検討事例一覧)

ANNEX 5-1: Case studies (OECD)

EXAMPLES OF CATEGORY APPROACHES

1. Examples presented in this Annex are chemicals being investigated in the OECD HPV Chemicals Programme. They have been shortened for purposes of presentation in this document to illustrate the steps for identification and development of categories included in this guidance document. The examples are:

- A. Alpha-olefins - discrete chemicals with an incremental and constant change across the category;
- B. Linear alkyl benzenes - family of mixtures; and
- C. Brominated diphenyl ethers - family of congeners.
- D. Butenes – family of isomers and their mixtures
- E. Hydrocarbon solvents – family of complex mixtures
- F. Inorganic nickel compounds

Example A: Alpha Olefins Series

Step 1: Identification of structure-based category and its members:

2. The category was defined as olefins bearing a single medium-length, even-numbered, unbranched aliphatic chain with no other functional groups ("α-Olefins"). This category consists of discrete chemicals with an incremental and constant change across its members (dimethylene group). Because the double bond is terminal, possible metabolic reactions such as oxidation at the double bond or allyl position should not be unduly affected by the chain lengthening. The lower (C_6) and upper (C_{14}) boundaries were based on the available product lines of the sponsors involved in the OECD effort.

3. The chemical structure of the category is:

R = CH_3, n-Propyl, n-Pentyl, n-Heptyl, n-Nonyl

Step 2: Gather published and unpublished literature for each category member.

4. A literature search resulted in identifying a significant amount of available data for most category members in most of the major SIDS endpoints.

Step 3: Evaluate available data for adequacy.

5. Available data was evaluated at the individual study level and collected for each member of the category. Available data were compiled and included all SIDS endpoints and other relevant information; non-SIDS data were found and used in the hazard profile (e.g., aspiration hazard potential to humans).

Step 4: Construct a matrix of data availability.

6. Table A-1 is a matrix of SIDS endpoints and available/adequate data for each member of the alpha-olefin category. For simplicity, not all relevant data are presented.

Step 5: Perform an internal assessment of the category.

7. The information in Table A-1 identifies where data gaps exist (noted as "-" in the table). Adequate data (noted as "√" in the table) are available for most endpoints. Endpoint data were evaluated to determine whether they correlate with chemical structure to judge the acceptability of the category. Although not shown in Table A-1, the data suggested that water solubility decreased with increasing chain length and aquatic toxicity appeared to decrease with increasing chain length.

Table A-1
STEP 4: Matrix of Available and Adequate Data on Alpha-Olefin Category Members

Test	Hexene	Octene	Decene	Dodecene	Tetradecene
Physicochemical Properties					
Partition Coeff.	√	-	√	√	-
Water Solubility	-	-	-	√	√
Environmental Fate					
Biodegradation	√	-	√	√	√
Ecotoxicity					
Acute Fish	√	-	√	√	-
Acute Daphnid	√	-	√	√	-
Alga	√	-	√	√	-
Terrestrial	-	-	√	-	-
Human Health Effects					
Acute Oral	√	√	√	√	√
Acute Inhalation	√	√	√	√	√
Acute Dermal	√	√	√	√	√
Repeated Dose	√	√	-	-	-
Genotoxicity (in vitro - bacteria)	√	√	√	√	√
Genotoxicity (in vitro - non-bacterial)	√	√	-	√	√
Genotoxicity (in vivo)	√	-	-	-	-
Repro/Developmental	-	-	-	-	-

(√) = Data available and considered adequate; (-) = No data available, or available data considered inadequate.

Step 6: Prepare category test plan.

8. Table A-2 contains the proposed testing plan only for the endpoints for which new testing was recommended for the alpha-olefins. In this case it appears reasonable that if data gaps are filled by testing at the upper and lower ends of the homologous series (shaded regions in the table), and if the results suggest a pattern, then the remaining data gaps can be considered to fall within the ranges defined by the data.

Step 7: Conduct necessary testing.

9. The shaded cells in Table A-2 show where new testing was recommended for the category.

Table A-2
Alpha-Olefin Proposed SIDS Test Plan[1]

Selected SIDS Endpoint	Hexene	Octene	Decene	Dodecene	Tetradecene
Water Solubility	√/-	-	-	√/+	√/+
Acute Fish	√/+	-	√/+	√/+	-
Acute Daphnid	√/+	-	√/+	√/+	-
Acute Algae	√/+	-	√/+	√/+	-
Repeated Dose	√/+	√/+	-	-	-[2]
Repro/Developmental	-	-	-	-	-[2]

[1] KEY: √/- = data available, but not adequate; √/+ = data available and considered adequate; - = no data available. Shaded cells represent those SIDS endpoints for which testing was recommended.
[2] A combined repeated dose and reproductive/developmental toxicity screen study design was recommended.

Step 8: Perform an external assessment of the category.

10. Table A-3 shows the results of the recommended testing and how it "fit" with available data for purposes of evaluating whether a pattern exists between some of the SIDS endpoints and the increase in 2-carbon increments from hexene to tetradecene. Note that there are four data points that exist in Table A-3 that were not present in Table A-2 (the octene water solubility and ecotoxicity results); these data were a late addition to the octene dossier and are included here to enhance the category analysis. This illustrates how all data should be considered in the evaluation of a category, even if it becomes available well after the literature search has been completed.

11. The new data show that patterns are clearly evident. For example, there is an apparent decrease in water solubility with increase in carbon chain length and a decrease in acute toxicity to fish and daphnids with an increase in carbon chain length. On the other hand, the mammalian toxicity data suggest a pattern of no difference between hexene and tetradecene for repeated dose (general) toxicity and developmental/ reproductive toxicity.

Table A-3
Results and Interpolation of Alpha-olefin SIDS Category Testing[1]

Selected SIDS Endpoint	Hexene	Octene	Decene	Dodecene	Tetradecene
Water Solubility	50 mg/L[2]	(4.1 mg/L)[3]	INSOLUBLE	"insoluble"	0.0004 mg/L
Acute Fish	5.6 mg/L (LC_{50})	(4.8 mg/L)[3] (LC_{50})	>Water solubility? (Reported value >10,000 mg/L (LC_{50})	>Water solubility? (Reported value >1000 mg/L (LC_{50})	>Water solubility (LC_{50})
Acute Daphnid	10 mg/L (NOEC)	(3 < EC_{50} > 10)[3]	>Water solubility? (EC_{50})	>Water solubility? (EC_{50})	>Water solubility (LC_{50})
Acute Algae	>Water solubility (LC_{50})	(>Water solubility)[3] (LC_{50})	>Water solubility? (EC_{50})	>Water solubility? (EC_{50})	>Water solubility (LC_{50})
Repeated Dose	$NOEL_{oral}$ = 101 mg/kg (males) and >1000 mg/kg (females)	NOEL = 50 mg/kg (males)	SIMILARLY TOXIC		$NOEL_{oral}$ = 100 mg/kg (males) and >1000 mg/kg (females)
Repro/ Developmental	$NOEL_{repro}$ and $NOEL_{dev}$ = >1000 mg/kg	SIMILARLY TOXIC			$NOEL_{repro}$ and $NOEL_{dev}$ = >1000 mg/kg

[1] KEY: - = no data available; shaded cells represent those SIDS endpoints for which OECD recommended testing.
[2] Apparently this was the original value thought not adequate, but estimations of the water solubility were similar to this value, so a new study was not performed.
[3] These data were not identified as being available in the Testing Plan. However, because they were reported in the dossier, they are included here to enhance the category analysis.

Step 9: Fill the data gaps

Water solubility.

12. The 50 mg/L value for hexene and 0.0004 mg/L value for tetradecene suggest a wide range of solubility for the five members of the group. The octene value of 4.1 mg/L suggests that the pattern (decreasing water solubility with increasing chain length) holds. Therefore, water solubility tests were judged not necessary and computer estimates (consistent with the latter premise for decene and dodecene) were considered acceptable.

Acute aquatic toxicity

13. The data in Table A-3 suggests that hexene and octene may exhibit moderate acute toxicity to fish and daphnids based on measured values (NOEC, LC_{50}, EC_{50}). However, all other members of the category appear to show no effects on fish and daphnids at saturation. In the case of algae, all category members show no effects at saturation. From a category perspective, it appears that a declining pattern

exists for fish and daphnids (hexene and octene are more toxic than decene, dodecene, and tetradecene) but there was a flat pattern for algae (all members appeared equal). Based on this information, it was decided that no additional aquatic toxicity testing was necessary. The three literature values for octene noted in Table A-3 were considered acceptable. The aquatic acute toxicity for those endpoints correlate with water solubility, which in turn appear to determine (or limit) bioavailability of octene.

Repeated dose toxicity

14. The results presented in Table A-3 suggest that the general toxicity of hexene and tetradecene are similar, whereas octene appears more toxic than either hexene or tetradecene. In both cases, male rats were more sensitive than female rats. The effect observed in males, a male-rat specific kidney effect, does not appear to be relevant to humans. Also, both studies followed the OECD repeated dose/reproductive/developmental toxicity screening testing protocol. There were no data for either decene or dodecene. The octene data point suggests that any category pattern that might exist (equal toxicity across all members) given the hexene and tetradecene data might not exist for the middle members of the category. However, upon closer inspection of the octene data in the octene dossier, it is seen that the doses used in the repeated-dose study were 5, 50, and 500 mg/kg. Since the LOEL was 500 mg/kg, the "true" NOEL is anywhere from 50 to 500. Therefore, given these data, one could recommend that all members of the group likely have equal general toxicity under repeated dose conditions and testing of decene and dodecene is not required.

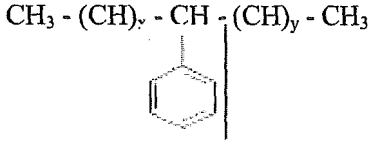
Reproductive/Developmental toxicity

15. The reproductive/developmental toxicity row in Table A-3 shows that data are available only for hexene and tetradecene. As with the repeated dose data, the results of the two studies were essentially the same. This suggests that it would not be necessary to test the middle three members of the category (octene, decene, and dodecene), especially given the results of the assessment of general toxicity (see above). The data suggest a consistent pattern across the category, or that all members are equally toxic for reproductive/ developmental effects under the conditions of the hexene/tetradecene studies (highest dose of 1000 mg/kg).

Example B: Linear Alkylbenzenes

Step 1: Identification of structure-based category and its members:

16. The linear alkylbenzene (LAB) category is comprised of nine different commercial formulations. Each formulation is a mixture containing various proportions of individual LABs with the following formulae:



Where x + y = 7-13 and x = 0-7, giving a linear carbon range of C_{10} to C_{16}.

17. Thus, this category would fall under "family of mixtures" in terms of category type. Table B-1 presents the nine commercial products evaluated. Note that the LAB category may be further subdivided into three subcategories based on the percentage of alkyl substituents with a low (C_{10}-C_{11}), mid (C_{11}-C_{13}), and high (C_{13}-C_{14}) proportion of carbon chain lengths.

Table B-1
Assignment of LAB SubCategories[1]

LAB Formulation	Carbon Chain Length for Substituted Alkyl Group (Numbers represent percent of total)				
	C_{10}	C_{11}	C_{12}	C_{13}	C_{14}[(2)]
Nalkylene 500	21	39	31	7	<1
Nalkylene 500L	20	44	31	5	<1
Alkylate 215	16	43	40	1	<1
Nalkylene 550L	14	30	29	20	7
Alkylate 225	7	25	48	19	1
Nalkylene 575L	9	17	20	30	15
Nalkylene 600	<1	1	23	50	25
Nalkylene 600L	<1	1	23	50	25
Alkylate 230	1	2	16	50	30

1 The two shaded regions and the open area make three subcategories by presenting two ends of the spectrum in terms of a higher proportion (>50%) of shorter carbon chains (upper left) and a higher proportion (>50%) of longer carbon chains (lower right). Bolded formulations had available data in all SIDS categories.
2 The proportion of C_{15} and C_{16} is < 1% in all formulations except for an incidence of 1% C_{15} in Alkylate 230.

Step 2: Gather published and unpublished literature for each category member.

18. A literature search resulted in identifying data for most category members in the environmental fate, ecotoxicity and human health effect SIDS endpoints.

Step 3: Evaluate available data for adequacy.

19. Again, as was discussed in the alpha-olefin example, evaluation of data adequacy is performed at the individual study level. [Guidance for Determining the Quality of Data for the SIDS Dossier (Interim SIDS Manual)]

Step 4: Construct a matrix of data availability.

20. An analysis of available data resulted in a matrix as presented in Table B-2. Again, for simplicity not all data found or compiled are presented here. Note that three LAB formulations (Alkylate 215, Alkylate 225, and Alkylate 230) had data available in each of the major SIDS classes (environmental fate, ecotoxicity, and health effects), and they each represent one of the three subcategories presented in Table B-1.

Table B-2
STEP 4: Matrix of Available and Adequate Data on LAB CategoryMembers[1]

LAB Formulation	Environ-mental Fate	Ecological Effects			Human Health Effects			
		Fish Acute	Daphnid Acute	Daphnid Chronic	Acute[4]	Repeated Dose[5]	Mutagen-icity[6]	Develop-mental[7]
Nalkylene 500	-				√	-		
Nalkylene 500L					-			
Alkylate 215	√	√	√	√	√	-	√	√
Nalkylene 550L	-				√	-		
Alkylate 225	√	√	√	-	√	√	√	-
Nalkylene 575L	-				-			
Nalkylene 600	-				√	-		
Nalkylene 600L					√			
Alkylate 230	√	√	√	√	√	√	√	√

[1] "√" denotes data are available and adequate. "-" denotes data are either not available, or are available and are judged inadequate. Shaded areas mark the three subcategories identified in Table B-1.

Step 5: Perform an internal assessment of the category.

21. As with Table A-1 in the alpha-olefin example, the data in Table B-2 identifies where data gaps exist. Note that adequate data are available for most endpoints for the three LAB formulations mentioned above. Table B-3 is essentially the same table as Table B-2, except that the data values are placed in each cell so that they can be evaluated to determine the acceptability of the category approach for each endpoint.

22. Table B-3 shows a consistent pattern of no discernible difference in aerobic degradation among the three LAB formulations tested (range of 56% - 61% of parent material evolved as carbon dioxide after a 35 day incubation period). Similarly, the acute fish toxicity, chronic daphnid toxicity, acute mammalian toxicity, reproductive/developmental toxicity, and mutagenicity data do not show differences across the tested formulations. However, the acute daphnid toxicity results, as well as the repeated dose toxicity tests in mammals suggest a pattern of increasing toxicity with an increase in the proportion of higher length carbon chains in the substituted alkyl group that appears to hold for each of these SIDS endpoints.

Step 6, 7 and 8: Prepare category test plan for review; Conduct necessary testing; and Perform an external assessment of the category.

23. In this case, it was concluded that no further testing was necessary under the SIDS programme and that the existing data were sufficient for a screening level hazard assessment. Thus; it was not deemed necessary to test each LAB formulation given the results of testing in three separate formulations to represent the boundaries of the category.

24. In this example, the test plan would include the rationale for "no testing" together with an evaluation of the existing data. Robust summaries for the individual supporting studies would also be available.

Table B-3
Evaluation of Matrix Data Patterns for LAB Category

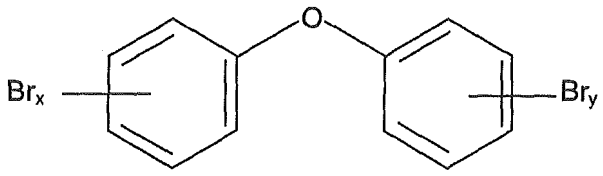
LAB Formulation	Environmental Fate	Ecological Effects			Human Health Effects			
		Fish Acute	Daphnid Acute	Daphnid Chronic	Acute[4]	Repeated Dose[5]	Mutagen-icity[6]	Develop-mental[7]
Nalkylene 500	Not tested	Not tested			>34 g/kg	Not tested		
Nalkylene 500L					Not tested			
Alkylate 215	**56%[1]**	**> Water solubility**	**80 ppb[2]**	**7.5 to 15 ppb[3]**	**17 g/kg**	**100 mg/m³**	**Negative**	**125 mg/kg**
Nalkylene 550L	Not tested	Not tested			>5 g/kg	Not tested		
Alkylate 225	**61%[1]**	**> Water solubility**	**9 ppb[2]**	**Not tested**	**28 g/kg**	**29 mg/m³**	**Negative**	**Not tested**
Nalkylene 575L	Not tested	Not tested			Not tested			
Nalkylene 600	Not tested	Not tested			>35 g/kg	Not tested		
Nalkylene 600L					>5 g/kg			
Alkylate 230	**56%[1]**	**> Water solubility**	**10 ppb[2]**	**13 to 23 ppb[3]**	**21 g/kg**	**<32 mg/m³**	**Negative**	**125 mg/kg**

[1] Percent of parent material evolved as carbon dioxide after 35 days in an aerobic biodegradation test.
[2] 48-hour LC_{50}s.
[3] 21-Day No Observed Effect Concentration (NOEC).
[4] Oral LD_{50}s in rodents.
[5] Four week inhalation studies in rats, values represent NOECs for the following effects: irritation of the eyes and nose and decreased body weight.
[6] Negative in vitro (bacteria - Ames; mammalian - Chinese hamster ovary cells) and in vivo (chromosomal aberration study in rats) tests.
[7] Developmental toxicity study (oral, rats, doses of 0, 125, 500, and 2000 mg/kg/d). Numbers in column represent no observed adverse effect level (NOAEL) for both maternal (weight gain) and developmental (ossification variations) endpoints.

Example C: Brominated Diphenyl Ethers

Step 1: Identification of structure-based category and its members:

25. The polybrominated diphenyl ether (PBDE) category theoretically contains a number of congeners (mono- through to decabromodiphenyl ether) but only three products are produced commercially: bis (pentabromophenyl) ether, also known as decabromodiphenyl ether (decaBDE); diphenyl ether, octabromo derivative (octaBDE); and diphenyl ether, pentabromo derivative (pentaBDE). The general chemical formula for this category is:



$x + y = 5, 8, 10$

26. This category is the "family of congeners" category type and is limited to three products produced commercially as most of the laboratory test data has been obtained with these products. DecaBDE is an essentially pure substance, but the other two are complex mixtures of related substances with varying degrees of bromination and substitution patterns. The actual compositions of the commercial products are summarised in table C-1. This particular example is limited to an analysis of ecotoxicity data.

Table C-1
STEP 1: Typical compositions of commercially available PBDEs

Congener	PentaBDE	OctaBDE	DecaBDE
tribromo-	0-1%		
tetrabromo-	24-38%		
pentabromo-	50-62%	1.4-12%[1]	
hexabromo-	4-12%		
heptabromo-	trace	43-58%	
octabromo-		26-35%	
nonabromo-		8-14%	≤3%
decabromo-		0-3%	≥97%

[1]This figure refers to the combined total of pentabromo- and hexabromo- congeners present.

Step 2: Gather published and unpublished literature for each category member.

27. A literature search identified some ecotoxicity data for all category members.

Step 3: Evaluate available data for adequacy.

28. As with the other examples in this Appendix, evaluation of data adequacy is performed at the individual study level.

Step 4: Construct a matrix of data availability.

29. Table C-2 presents a matrix for the available ecotoxicity data based on the literature search. SIDS data gaps exist for acute invertebrate testing (decaBDE) and for acute algal testing (octaBDE).

Table C-2
STEP 4: Available Acute Ecotoxicity Data on PBDEs[1]

Test Organism	PentaBDE	OctaBDE	DecaBDE
Fish	√	√	√
Invertebrate	√	√	-
Algae	√	-	√

1 "√" denotes data available and adequate; "-" denotes data not available, or available and not adequate.

Step 5: Perform an internal assessment of the category.

30. Table C-3 is essentially the same table as Table C-2, except that actual data replace the "√s".

31. In evaluating these data, it was concluded that a decrease in aquatic toxicity could be expected with increasing bromine number. Since there were adequate aquatic toxicity data for the category member with the lowest number of bromine atoms (pentaBDE), it was not necessary to conduct additional acute toxicity tests on the remaining members with a higher number of bromine atoms. DecaBDE would not be more toxic to invertebrates than octaBDE, and the algal toxicity of octaBDE could be inferred from the data on penta- and decaBDE.

32. In addition to the ecotoxicity data, available data on environmental monitoring, bioconcentration, and the physicochemical properties of the category members were evaluated. It was determined that there was a decreasing concern for bioaccumulation potential with an increase in bromine number; that all three compounds were not very water soluble; and that they all had high octanol-water partition coefficients (log K_{ow}). This suggested that the likely exposure scenario of concern would be to organisms exposed directly to sediment or soil.

Table C-3
Available Acute Ecotoxicity Data on PBDEs

Test Organism	PentaBDE	OctaBDE	DecaBDE
Fish	Rainbow trout NOEC (96 hr) = 21 µg/L (>water solubility?)	Medaka LC_{50} (48 hr) = >water solubility	Medaka LC_{50} (48 hr) = >water Solubility
	Medaka LC_{50} (48 hr) = > water solubility		
Invertebrate	Daphnid EC_{50} (48 hr) = 14 µg/L NOEC (48 hr) = 4.9 µg/L (EC_{50} values close to water solubility)	Daphnid 21-day NOEC > 2 µg/L	No Data
Algae	*Selanastrum capricornutum* NOEC (96 hr) up to 26 µg/L (>water solubility?)	No Data	Three different species EC_{50} (72 hr) > water solubility

[1] Small freshwater fish (warm water species).

Step 6: Prepare category test plan for review.

33. Because of the concern for bioaccumulation and partitioning of thePBDEs to the sediment/soil environment, it was recommended that further testing (chronic aquatic toxicity, sediment toxicity, and soil toxicity) be conducted, begining with pentaBDE. Therefore, the final testing recommendation required "advanced" SIDS testing without filling the acute aquatic toxicity basic SIDS data gaps. The testing plan (Table C-4) was tiered, the results of the lower tiers determining the next set of tests.

Table C-4
OECD SIDS Proposed Ecotoxicity Testing Plan withPBDEs

Tier	Category Member	Ecotoxicity Test[1]	Result	Comment
I	PentaBDE	Fish early life stage test	Rainbow trout 60-day NOEC = 8.9 µg/l	Fish test to verify bioaccumulative potential.
		Daphnid reproduction test	Daphnid 21-day NOEC = 5.3 µg/l	Daphnid study to verify that acute effects were due to toxicity.
		Sediment (midge) toxicity test	*Chironomus riparius* 28-day NOEC = 16 mg/kg dry weight	To verify concerns identified in hazard/exposure assessment
		Sediment (oligochaete) toxicity test	*Lumbriculus variegatus* 28-day NOEC = 3.1 mg/kg dry weight	
		Sediment (amphipod) toxicity test	*Hyalella azteca* 28-day NOEC ~ 6.3 mg/kg dry weight	
		Soil (earthworm) toxicity test	*Eisenia fetida* 14-day NOEC >500 mg/kg dry weight	
		Soil (plant) toxicity test	Six plants – lowest 21-day EC_5 = 16 mg/kg dry weight	
		Soil (nitrification inhibition) toxicity test	Soil microorganisms 28-day NOEC ≥ 1 mg/kg dry weight	
II	OctaBDE	Sediment (oligochaete) toxicity tests using two sediment types	*Lumbriculus variegatus* 28-day NOEC ≥ 1,272 mg/kg dry weight	Tests were chosen based on the pentaBDE results – for example, sediment organism sensitivity is not expected to differ significantly and so only the most sensitive organism from the pentaBDE test series required testing.
		Soil (earthworm) toxicity test	*Eisenia fetida* 56-day NOEC ≥ 1,470 mg/kg dry weight	
		Soil (plant) toxicity test	Six plants – 21-day NOEC ≥ 1,190 mg/kg dry weight	
III	DecaBDE	Sediment (oligochaete) toxicity tests using two sediment types	*Lumbriculus variegatus* 28-day NOEC ≥ 3,841 mg/kg dry weight	As for octaBDE
		Soil (earthworm) toxicity test	*Eisenia fetida* 56-day NOEC ≥ 4,910 mg/kg dry weight	
		Soil (plant) toxicity test	Six plants – 21-day NOEC ≥ 5,349 mg/kg dry weight	

[1] All tests are beyond the basic SIDS requirements. The testing plan is presented to show how basic SIDS requirements were waived in order to proceed to a more meaningful testing scheme.